Exploring the Fate of Nitrogen Heterocycles in Complex Prebiotic Mixtures

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A long standing question in the field of prebiotic chemistry is the origin of the genetic macromolecules DNA and RNA. DNA and RNA have very complex structures with repeating subunits of nucleotides, which are composed of nucleobases (nitrogen heterocycles) connected to sugar-phosphate. Due to the instability of some nucleobases (*e.g.* cytosine), difficulty of synthesis and instability of D-ribose, and the likely scarcity of polyphosphates necessary for the modern nucleotides, alternative nucleotides have been proposed for constructing the first genetic material (Joyce *et al.*, 1987). Thus, we have begun to investigate the chemistry of nitrogen heterocycles in plausible, complex prebiotic mixtures in an effort to identify robust reactions and potential alternative nucleotides.

We have taken a complex prebiotic mixture produced by a spark discharge acting on a gas mixture of N_2, CO_2, CH_4, and H_2, and reacted it with four nitrogen heterocycles: uracil, 5-hydroxymethyluracil, guanine, and isoxanthopterin (2-amino-4,7-dihydroxypteridine) (Figure 1). The products of the reaction between the spark mixture and each nitrogen heterocycle were characterized by liquid chromatography coupled to UV spectroscopy and Orbitrap mass spectrometry. We found that the reaction between the spark mixture and isoxanthopterin formed one major product, which was a cyanide adduct. 5-hydroxymethyluracil also reacted with the spark mixture to form a cyanide adduct, uracil-5-acetonitrile, which has been synthesized previously by reacting HCN with 5-hydroxymethyluracil (Robertson and Miller, 1995). Unlike isoxanthopterin, the chromatogram of the 5-hydroxymethyluracil reaction was much more complex with multiple products including spark-modified dimers. Additionally, we observed that HMU readily self-polymerizes in solution to a variety of oligomers consistent with those suggested by Cleaves (2001). Guanine and uracil, the biological nucleobases, did not react with the spark mixture, even at high temperature (100 °C). This suggests that there are alternative nucleobases which are more reactive under prebiotic conditions and may have been involved in producing precursor nucleotides.

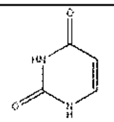
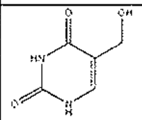
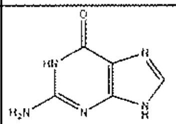
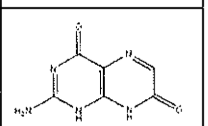
NAME	uracil	5-hydroxy-methyluracil	guanine	isoxanthopterin
STRUCTURE				
RESULT	unreactive	*reactive*	unreactive	*reactive*

Figure 1. Structures of the four nitrogen heterocycles that were reacted with a complex mixture produced by a spark discharge apparatus. Significant reaction was only observed for 5-hydroxymethyluracil and isoxanthopterin.

References

Cleaves, HJ (2001) Studies in Prebiotic Synthesis and the Origins of the Metabolic Pathways. Diss. University of California, San Diego.

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Robertson, MP and Miller, SL (1995) Prebiotic Synthesis of 5-Substituted Uracils: A Bridge Between the RNA World and the DNA-Protein World. *Science*, 268: 702-705.